

IN THE CLAIMS:

1-7. (Withdrawn)

8. (Currently amended) A differentiated committed human progenitor cell line capable of differentiation and propagation into mature neurons or glial cells, said cell line derived from undifferentiated pluripotent human embryonic stem cells *in vitro*.

9. (Original) The differentiated committed human progenitor cell line according to claim 8 capable of establishing a graft in a recipient brain.

10. (Original) The differentiated committed human progenitor cell line according to claim 9 capable of differentiating *in vivo* into other cell lineages including neurons and glial cells such as astrocytes and oligodendrocytes.

11. (Currently amended) A neural progenitor cell differentiated *in vitro* from an undifferentiated pluripotent human embryonic stem cell.

12. (Original) The neural progenitor cell according to claim 11 wherein said cell is capable of proliferation.

13. (Original) The neural progenitor cell according to claim 11 wherein said cell is capable of differentiating to a mature neuron cell or glial cell.

14. (Currently amended) The neural progenitor cell according to claim 11 wherein said cell is capable of transdifferentiation into other progenitor cell lineages to generate stem cells and differentiated cells of non-neural phenotype.

15. (Original) The differentiated neural progenitor cell according to claim 8 or 11 characterised by expressed markers including markers of the neuroectodermal lineage; markers

of neural progenitor cells; neuro-filament proteins; monoclonal antibodies including MAP2ab; glutamate; synaptophysin; glutamic acid decarboxylase; tyrosine hydroxylase; β -tubulin; β -tubulin III; GABA A α 2 receptor, glial fibrillary acidic protein (GFAP), galactocerebroside (gal C), 2', 3'- cyclic nucleotide 3'- phosphodiesterase (CNPase), *plp*, DM-20 and O4.

16. (Original) The neural progenitor cell according to claim 15 which expresses markers of neuroectoderm and neural progenitor cells selected from the group including NCAM, nestin, vimentin and the transcriptional factor Pax-6, and do not express Oct-4.

17. (Original) The neural progenitor cell according to claim 16 wherein said cell is capable of establishing a graft in a recipient brain.

18. (Original) The neural progenitor cell according to claim 17 wherein said cell can incorporate extensively into a recipient brain.

19. (Original) The neural progenitor cell according to claim 18 wherein said cell is capable of migrating along host brain pathways.

20. (Currently amended) The neural progenitor cell according to claim 19 wherein said cell ~~is responsive~~ differentiates in response to host environmental signals.

21. (Original) The neural progenitor cell according to claim 20 wherein said cell differentiates in response to local host environmental signals.

22. (Original) The neural progenitor cell according claim 20 wherein said cell is capable of differentiation to other cell lineages in a recipient brain.

23. (Currently amended) The ~~enriched preparation of~~ neural progenitor cells ~~including an enriched population of cells~~ according to claim 15, wherein said neural progenitor cells constitute an enriched preparation.

24. (Original) The enriched preparation of neural progenitor cells according to claim 23 wherein said cells are capable of prolonged undifferentiated proliferation.
25. (Original) The enriched preparation of neural progenitor cells according to claim 23 wherein said cells are capable of differentiation into neurons, mature neurons and glial cells.
26. (Original) The enriched preparation of neural progenitor cells according to claim 25 wherein said cells are capable of establishing a graft in a recipient brain in the absence of tumors.
27. (Currently amended) The enriched preparation of neural progenitor cells according to claim 26 wherein said cells ~~may be~~ is recovered from cryopreservation.

28-38. (Withdrawn)

39. (Currently amended) A method of inducing somatic differentiation of stem cells *in vitro* into progenitor cells said method comprising:
obtaining undifferentiated human pluripotent embryonic stem cells; and
providing a controlled differentiating ~~signal under~~ conditions which ~~are~~ is non-permissive for stem cell renewal, does not kill cells ~~and/or~~ induces unidirectional differentiation toward extraembryonic lineages.

40. (Currently amended) The method according to claim 39 wherein said undifferentiated pluripotent embryonic stem cell is capable of proliferation *in vitro* and differentiation to neural progenitor cells, neuron cells or glial cells and is immunoreactive with markers for human pluripotent stem cells including SSEA-4, GCTM-2 antigen, and TRA 1-60.

41. (Currently amended) The method according to claim 39 wherein said undifferentiated pluripotent embryonic stem cell expresses Oct-4.

42. (Currently amended) The method according to claim 39 wherein said undifferentiated pluripotent embryonic stem cell maintains a diploid karyotype during prolonged cultivation ~~in~~

vivo in vitro.

43. (Currently amended) The method according to claim 39 wherein said undifferentiated pluripotent embryonic stem cell forms tumors when injected in the testis of immunodeprived SCID mice.

44. (Currently amended) The method according to claim 39 wherein said undifferentiated human pluripotent embryonic stem cell is prepared according to ~~the~~ a method of claim 28 comprising:
obtaining an *in vitro* fertilised human embryo and growing the embryo to a blastocyst stage of development;

removing inner cells mass (ICM) cells from the embryo;

culturing ICM cells under conditions which do not induce extraembryonic differentiation and cell death, and promote proliferation of undifferentiated stem cells; and
recovering stem cells.

45. (Currently amended) The method according to claim 39 44 wherein said undifferentiated human pluripotent embryonic stem cell is prepared ~~according to the method of claim 37.~~ further comprising:

culturing the ICM cells on a fibroblast feeder layer to promote proliferation of embryonic stem cells prior to recovering the stem cells from the feeder layer, wherein the fibroblast feeder cells are arrested in their growth.

replating the stem cells from the fibroblast feeder layer onto another fibroblast feeder layer;
and

culturing the stem cells for a period sufficient to promote proliferation of morphologically undifferentiated stem cells.

46. (Currently amended) The method according to claim 39 wherein the conditions for inducing somatic differentiation of stem cells are selected from any one of the following including:

culturing the undifferentiated stem cells for prolonged periods and at high density on a fibroblast feeder cell layer to induce differentiation;

culturing the undifferentiated stem cells in serum free media;
culturing the undifferentiated stem cells on a differentiation inducing fibroblast feeder layer and wherein said fibroblast feeder layer does not induce extra embryonic differentiation and cell death;
culturing to a high density in monolayer or on semi-permeable membranes so as to create structures ~~mimieing~~ mimicking the postimplantation phase of human development; or
culturing in the presence of a chemical differentiation factor selected from the group including bone morphogenic protein-2 or antagonists thereof.

47. (Original) The differentiated progenitor cell prepared by the method according to claim 39.

48. (Original) The differentiated progenitor cell according to claim 47 selected from the group including a neural progenitor cell or mesodermal progenitor cell including hemangioblast or hematopoietic stem cells.

49. (Original) The differentiated progenitor cell according to claim 48 which is a neural progenitor cell capable of differentiating into a neuron cell or a glial cell.

50. (Currently amended) A method of inducing differentiation of somatic progenitors to somatic cells from embryonic stem cell derived somatic progenitors, wherein said progenitors are derived from human pluripotent embryonic stem cells *in vitro*, said method comprising:

obtaining a source of embryonic stem cell derived somatic progenitors; culturing the progenitor cells on an adhesive substrate; and

inducing the cells to differentiate to somatic cells under conditions which favour somatic differentiation.

51. (Original) The method according to claim 50 wherein said embryonic stem cell derived somatic progenitor cells are grown in the presence of a serum free media and growth factors and are induced to differentiate by withdrawal of the growth factors.

52. (Original) The method according to claim 50 wherein the embryonic stem cell-derived progenitor cell is prepared according to the method of claim 39.

53. (Original) The method according to claim 50 wherein the embryonic stem cell-derived progenitor cell is selected from the group consisting of a neural progenitor cell or mesodermal progenitor cell including hemangioblast or hematopoietic stem cells.

54. (Original) The method according to claim 50 wherein the embryonic stem cell-derived progenitor cell is a neural progenitor cell capable of differentiating into a neuron cell or a glial cell.

55. (Original) The method according to claim 54 wherein the progenitor cells are cultured on an adhesive substrate selected from poly-D-lysine and laminin or poly-D-lysine and fibronectin.

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Cont 56. (Original) The method according to claim 55 wherein the progenitor cells are cultured on poly-D-lysine and laminin.

57. (Original) The method according to claim 56 wherein the cells are further cultured in the presence of retinoic acid.

58. (Currently amended) The method according to any one of claims 55 to 57 wherein said somatic cells ~~induced~~ are neurons including mature neurons.

59. (Original) The method according to claim 55 wherein the progenitor cells are cultured on poly-D-lysine and fibronectin.

60. (Original) The method according to claim 59 wherein the progenitor cells are cultured before and after plating on poly-D-lysine and fibronectin in serum free medium in the presence of PDGF-AA and bFGF.

61. (Original) The method according to claim 60 wherein the progenitor cells are cultured

after plating in the presence of PDGF-AA, basic FGF and EGF .

62. (Original) The method according to claim 61 further including culturing the somatic progenitor cells after plating in the presence of T3.

63. (Original) The method according to claim 62 wherein said somatic cells induced are glial cells including astrocyte and oligodendrocyte cells.

64. (Currently amended) A method of producing an enriched preparation of human pluripotent ES cell derived neural progenitor cells, said method comprising:

obtaining an undifferentiated human embryonic stem cell comprising obtaining an *in vitro* fertilised human embryo and growing the embryo to a blastocyst stage of development;

removing inner cells mass (ICM) cells from the embryo;

culturing ICM cells under conditions which do not induce extraembryonic differentiation and cell death, and promote proliferation of undifferentiated stem cells;

recovering stem cells;

inducing somatic differentiation of the embryonic stem cell to a neural progenitor cell comprising obtaining undifferentiated embryonic stem cells;

providing a differentiating signal under conditions which are non-permissive for stem cell renewal, do not kill cells or induces unidirectional differentiation toward extraembryonic lineages;

identifying a neural progenitor cell by expressed markers of primitive neuroectoderm and neural stem cells such as polysialyated N-CAM, intermediate filament proteins such as nestin and vimentin and the transcription factor Pax-6; and

culturing the neural progenitor cells to promote proliferation and propagation.

65. (Original) The method according to claim 64 wherein the neural progenitor cells are cultured as spheres or monolayers in serum free medium comprising DMEM/F12 supplemented with growth factors.

66. (Original) The method according to claim 65 wherein the growth factors include B27,

EGF and bFGF.

67. (Original) The method according to claim 66 including further culturing to eliminate non-neural cells, said culturing comprising further selective culturing in serum free media including DMEM/F12 supplemented with growth factors.

68. (Original) The method according to claim 67 wherein the further culturing includes the transfer of undifferentiated ES cell clumps into serum free medium comprised of DMEM/F12 supplemented with B27, bFGF and EGF and cultivation of the resulting neural progenitors as spheres or monolayers.

69-85. (Withdrawn)
